REMARKS

Claims 1-11 are pending.
Claims 2, 5 and 9-11 are withdrawn.
Claims 9-11 are withdrawn-currently amended.
Claims 1 is amended.
Claims 6 and 7 are cancelled.
Claims 1, 3, 4 and 8 are examined on the merits.
Claims 1, 3, 4 and 6-8 are rejected.

Specification

Although there is no requirement to supply section headings in an application, the applicants have amended the specification as requested by the examiner in order to progress the examination.

Further, applicants have amended the specification to add the current address of the depository collection on page 8.

NCIMB Ltd.
Ferguson Building
Crabstone Estate
Bücksburn, Aberdeen
Scotland, AB219YA

No new matter is added.

Claim Objections

Applicants have italicized the microorganism names in claims 1, 3, 4 and 8.

35USC 112, second paragraph

Claim 1 is amended to include the limitations of claims 6 and 7. As claims 6 and 7 no longer limit claim 1, they are cancelled. The term "obtainable" has been amended to read "obtained".

No new matter is added.

Applicants believe the amendment including the limitations of claims 6 and 7 serve to eliminate any indefiniteness of the present claims.

Examiner has rejected claims 3 and 4 because these contain parenthesis.

The terms "(meth)acrylonitile" and "(meth)acrylamide" are well known in the art. (Meth)acrylonitrile is a conventional way of referring to both methacryonitrile and acrylonitrile. (Meth)acrylamide is a standard way of referring to methacrylamide and acrylamide. As this is well known in the art, there is no indefiniteness about the terms "(meth)acrylonitile" and "(meth)acrylamide".

35 USC 112, first paragraph

Deposit

Please find enclosed herewith the deposit receipt and the viability statement for the strain NCIMB 41165 which describe all necessary items.

The material has been accepted for deposit under the Budapest treaty on the international Recognition of the Deposit of Microorganisms for the purpose of Patent Procedure and all restrictions on the availability to the public of the material so deposited will be irrevocably removed upon the granting of a patent.

35 USC 102(b)

Claims 1, 3, 4 and 6-8 are rejected under 35 USC 102(b) as being anticipated by Yamada (Biosci. Biotech. Biochem, 1996, 60((():1391-1400).

Examiner believes Yamada to anticipate even though Yamada makes no mention of the use of nitrile hydratase obtainable from a microorganism of the Dietzia genus.

Examiner is of the opinion that although the cited enzymes are not extracted from the cells belonging to Dietzia, the properties of the enzyme as intended for the claimed invention are not described in the as-filed specification and thus the differences, if any, cannot be established.

This seems to be an unreasonable rejection. Yamada discusses at length the screening of various organisms to find ones showing a high ability to produce acrylamide with less acrylic acid in the reaction mixtures. Among those organisms considered are *Pseudomonas chlororaphis* B23, *Rhodococcus rhodchrous* J1 and *Brevibacterium* R312. The various organisms, identified by their taxonomic designations are clearly different from one another in terms of activity and ability to form amide and acid product.

The microorganisms presently claimed in the process of the invention are selected from *Dietzia natronolimnaios* and *Dietzia psychralcaliphila*.

Clearly, *Dietzia natronolimnaios* and *Dietzia psychralcaliphila* have a different taxonomic designation than those discussed in Yamada and are therefore physically different. For example, *Pseudomonas* are Gram negative organisms, whereas *Dietzia* are Gram positive.

The present *Dietzia* microorganisms can be cultured at alkaline pHs, for instance pH 9 to 10 which facilitates improved sterility of the fermentation. See page 6, lines 27-28. Additionally, the *Dietzia* microorganisms have unexpectedly been found to exhibit high tolerance to high concentrations of unsaturated carboxylic acids and therefore enable ethylenically unsaturated amides, such as acrylamide, to be converted into a carboxylic acid, such as acrylic acid at high concentrations. See page 7, lines 2-5. Thus, the taxonomic designation of *Dietzia natronolimnaios* and *Dietzia psychralcaliphila* indicate the present microorganisms are physically different than those microorganisms described by Yamada. The microorganisms described by Yamada are highly sensitive to acrylic acid concentrations. In contrast, the present microorganisms exhibit properties highly advantageous to the production of ethylenically unsaturated amides in the presence of acrylic acids.

Further, Yamada describes the use of purified enzymes only. In contrast, the presently claimed process requires producing an ethylenically unsaturated amide wherein the nitrile is treated with an enzyme comprised <u>within</u> the whole cells of the microorganism. The applicants provide a process wherein the fermentation and bio-process can be integrated and thus carried out in a <u>single</u> step (cf. page 6, last paragraph of the present application).

Therefore, because there is no suggestion or teaching in Yamada to use enzymes obtained from a microorganism of a species of *Dietzia*,

- which is comprised within whole cells of the microorganism, and
- which is selected from the group consisting of *Dietzia natronolimnaios* and *Dietzia psychralcaliphila,*

there can be no anticipation.

35 USC 102(e)

Claims 1, 3, 4, 6 and 7 are rejected under 35 USC 102(e) as being anticipated by US 6,562,603 or US 6,916,638.

US 6,562,603

Examiner believes US 6,562,603 to anticipate and refers to col. 18, lines 11-26 in particular. Applicants respectfully disagree:

Example 15 shows the conversion of an hydroxyl nitrile to an acid, not the conversion of a nitrile to an ethyleneically unsaturated amide. Furthermore, there are no examples or suggestions within US '603 for making the presently claimed conversion.

Furthermore, US '603 makes no mention of microorganism selected from the group consisting of *Dietzia natronolimnaios* and *Dietzia psychralcaliphila* as presently claimed.

Thus the rejection is improper and there is no anticipation.

US6,916,638

Examiner believes this reference to anticipate. Applicants respectfully disagree for reasons similar to the arguments above.

The present method is directed to the preparation of an ethylenically unsaturated amide. No unsaturated amides are produced in US '638. There is no suggestion in US '638 to prepare ethyleneically unsaturated amides.

Furthermore, US '638 makes no mention of a microorganism selected from the group consisting of *Dietzia natronolimnaios* and *Dietzia psychralcaliphila* as presently claimed.

Thus there is no anticipation.

35 USC 103(a)

Claims 1, 3, 4 and 6-8 are rejected under 35 USC 103(a) as being unpatentable over Yamada or Nagasawa (Pure and Appl. Chem. 1995, 67(7):1241-1256) in view of US 6,562,603 and US 6,916,638.

The presently claimed process is directed to a process for producing an ethylenically unsaturated amide, wherein a nitrile is treated with an enzyme which is a nitrile hydratase in an aqueous medium, characterised in that
the nitrile hydratase is obtained from a microorganism of a species of *Dietzia*, which nitrile hydratase is comprised within whole cells of the microorganism, and which microorganism is selected from the group consisting of *Dietzia natronolimnaios* and *Dietzia psychralcaliphila*.

Examiner believes Yamada and Nagasawa teach conversion of acrylonitrile or (meth)acrylonitrile to acrylamide. Yamada and Nagasawa are silent about the enzymatic activity of *Dietzia*. Examiner alleges that US '603 and US '638 both teach that *Dietzia* has nitrile hydratase activity. Thus examiner believes it would be obvious to use the *Dietzia* microorganism having nitrile hydratase activity in the methods of Yamada and Nagasawa.

Applicants respectfully disagree for the reasons below.

US'603 or US'638 teach only that microorganisms of the *Dietzia* sp. ADL1 and *Dietzia maris* are suitable for the conversion of specific substituted nitriles, in particular of 3-hydroxynitriles and glycinonitrile. Both references disclose the conversion of nitriles to the acid. There is no verification of amide formation.

Neither documents teach or suggest the use of specific strains of the sp. *Dietzia natronolimnaios* or *psychralcaliphila*s.

The applicants enclose the taxonomic identification using the 16S rRNA technique carried out at the UK National Collection of Industrial and Marine Bacteria. According to the deposit receipt the analyzed strain BTR 2509 corresponds to the strain NCIMB 41165.

The closest match when compared with the Microseq™ database was a similarity of 98.44% with the sp. *Dietzia maris*. A further search against the public EMBL database identified the best match to *Dietzia natronolimnaios* with a similarity of 99.456%. Thus, there is a difference in the base pair sequence between the presently claimed microorganisms and those *Dietzia* microorganisms disclosed in US '603 and US '638.

Thus, even if Yamada and Nagasawa were combined with US '603 and US '638 , one does not arrive at the present process wherein the nitrile hydratase is obtained from a microorganism selected from the group consisting of *Dietzia natronolimnaios* and *Dietzia psychralcaliphila*.

Furthermore, applicants point out that US'603 converts 3-hydroxyvaleronitrile to 3-hydroxyvaleric acid. 3-hydroxyvaleric acid is not an ethylenically substituted amide. US '638 converts glycinonitrile to glycine. Glycine is neither an amide nor ethylenically unsaturated. There can be no expectation of success or motivation in using the microorganisms of US '603 or US '638 in the method of Yamada or Nagasawa because the substrates of US '603, 3-hydroxyvaleronitrile or US '638, glycinoitrile are entirely different than those of Yamada and Nagasawa. US'603 and US'638 do not teach the convertion of a nitrile to an ethylenically unsaturated amide but instead teach a convertion to either hydroxyvaleric acid or glycine. While there may be conversion to the acid in US '603 via an amide, there is no verification of amide formation in either US'603 or US '638 and certainly no teaching in either patent of formation of an ethylenically unsaturated amide.

Thus there can be no expectation of success or motivation to use the microorganisms of US '603 or US '638 in the method of Yamada or Nagasawa. Even if one skilled in the art were to combine the references, one does not arrive at the present process which requires a microorganism of the *Dietzia* genus selected from the group consisting of *Dietzia natronolimnaios* and *Dietzia psychralcaliphila*.

Reconsideration and withdrawal of the rejection of claims 1, 3, 4 and 8 is respectfully solicited in light of the remarks and amendments *supra* .

Since there are no other grounds of objection or rejection, passage of this application to issue with claims 1, 3, 4 and 8 is earnestly solicited.

Applicants submit that the present application is in condition for allowance. In the event that minor amendments will further prosecution, Applicants request that the examiner contact the undersigned representative.

Respectfully submitted,

Shiela A. Loggins

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540 White Plains Road
Tarrytown, New York 10591
(914) 785-2768

Shiela A. Loggins
Agent for Applicants
Reg. No. 56,221

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Enclosures: Petition for one (1) extension of time, Deposit receipt and the viability statement for the strain NCIMB 41165 which describe all necessary items and Microbial Identification for BTR2509.

BUDAPEST TREATY ON THE INTERNATIONAL RECOGNITION OF THE DEPOSIT OF MICROORGANISMS FOR THE PURPOSES OF PATENT PROCEDURE

CIBA Specialty Chemicals Water Treatments Ltd
P O Box 38
Cleckheaton Road
Low Moor
Bradford
BD12 0JZ

NAME AND ADDRESS OF THE PARTY TO WHOM THE VIABILITY STATEMENT IS ISSUED

INTERNATIONAL FORM

VIABILITY STATEMENT
issued pursuant to Rule 10.2 by the
INTERNATIONAL DEPOSITARY AUTHORITY
identified on the following page

I. DEPOSITOR	II. IDENTIFICATION OF THE MICROORGANISM
Name: AS ABOVE Address:	Accession number given by the INTERNATIONAL DEPOSITARY AUTHORITY: NCIMB 41165 Date of the deposit or of the transfer[1]: 5 March 2003

III. VIABILITY STATEMENT

The viability of the microorganism identified under II above was tested on 6 March 2003 [2]. On that date, the said microorganism was:

[3]

[X] viable

[ ] no longer viable

[1] Indicate the date of the original deposit or, where a new deposit or a transfer has been made, the most recent relevant date (date of the new deposit or date of the transfer).

[2] In the cases referred to in Rule 10.2(a)(ii) and (iii), refer to the most recent viability test.

[3] Mark with a cross the applicable box.

BUDAPEST TREATY ON THE INTERNATIONAL RECOGNITION OF THE DEPOSIT OF MICROORGANISMS FOR THE PURPOSES OF PATENT PROCEDURE

CIBA Specialty Chemicals Water Treatments Ltd
P O Box 38
Cleckheaton Road
Low Moor
Bradford
BD12 0JZ

INTERNATIONAL FORM

RECEIPT IN THE CASE OF AN ORIGINAL DEPOSIT
issued pursuant to Rule 7.1 by the
INTERNATIONAL DEPOSITARY AUTHORITY
identified at the bottom of this page

NAME AND ADDRESS OF DEPOSITOR

I. IDENTIFICATION OF THE MICROORGANISM

Identification reference given by the DEPOSITOR:	Accession number given by the INTERNATIONAL DEPOSITARY AUTHORITY:
Dietzia natronolimnaias BTR 2509	NCIMB 41165

II. SCIENTIFIC DESCRIPTION AND/OR PROPOSED TAXONOMIC DESIGNATION

The microorganism identified under I above was accompanied by:

[ ] a scientific description

[X] a proposed taxonomic designation

(Mark with a cross where applicable)

III. RECEIPT AND ACCEPTANCE

This International Depositary Authority accepts the microorganism identified under I above, which was received by it on 5 March 2003 (date of the original deposit)[1]

IV. RECEIPT OF REQUEST FOR CONVERSION

The microorganism identified under I above was received by this International Depositary Authority on (date of the original deposit) and a request to convert the original deposit to a deposit under the Budapest Treaty was received by it on (date of receipt of request for conversion)

V. INTERNATIONAL DEPOSITARY AUTHORITY

Name: NCIMB Ltd.,

Address: 23 St Machar Drive,
Aberdeen,
AB24 3RY,
Scotland.

Signature(s) of person(s) having the power to represent the International Depositary Authority or of authorised official(s): Terence Dundas

Date: 17 July 2003

[1] Where Rule 6/4(d) applies, such date is the date on which the status of International Depositary Authority was acquired.

Form BP/4 (sole page)

CONDITIONS UNDER WHICH THE VIABILITY TEST HAS BEEN PERFORMED[4]

V. INTERNATIONAL DEPOSITARY AUTHORITY	
Name: NCIMB Ltd., Address: 23 St Machar Drive, Aberdeen, A24 3RY, Scotland.	Signature(s) of person(s) having the power to represent the International Depositary Authority or of authorised official(s): Terence Daniels Date: 17 July 2003

[4] Fill in if the information has been requested and if the results of the test were negative.

NCIMB

Monday, March 04, 2002

Yvonne Armitage
CIBA Speciality Chemicals
PO Box 38,
Low Moor
Bradford
Yorkshire
BD12 0JZ

Dear Yvonne,
I am pleased to include further details of our extended data search on your three isolates as previously sent to you by Amelia.

NCSQ16677 BTR2509
99.456% similarity to *Dietzia natronolimnaea*
98.521% similarity to *Dietzia maris*

NCSQ16677 BTR2510
99.34% to both *Rhodococcus erythropolis* and *Nocardiodes simplex*.
Analysis of the cell wall for LDAP plus an examination for aerial mycelium would be needed to distinguish these two genera.

NCSQ16677 BTR 2511
99.271% similarity to both *Rh. erythropolis* and *N.simplex*.

When comparing Microseq and EMBL data it is important to remember that we have no control over the quality of the data submitted to EMBL, and that the taxonomic designation of the strains may not be entirely current.
A CD with full details of your analysis is enclosed.

Yours sincerely

Alison Baxter
Operations Manager

PROVIDING THE SOLUTION

NCIMB Ltd., 23 St Machar Drive, Aberdeen AB24 3RY, Scotland, UK
Tel: +44 (0) 1224 2733.42 Fax: +44 (0) 1224 272461 E-mail enquiries@ncimb.co.uk Website: http://www.ncimb.co.uk

Registered No. SCO 78368 Registered Office: 23 St Machar Drive, Aberdeen. NCIMB Limited

MICROBIAL IDENTIFICATION

MicroSeq™ Report Interpretation Guide

Methodology
The MicroSeq™ service is based on the identification of micro-organisms by the extraction of their DNA. The 16S rDNA gene is amplified from the extracted DNA by the Polymerase Chain Reaction (PCR) and the sequence determined using the dideoxy chain termination method. The DNA sequence of both the forward and reverse DNA strands is determined as a sequence quality check. These processes are carried out using NCIMB LTD's internal Work instructions as detailed in your report.

Data Analysis
The DNA sequence is searched against the MicroSeq™ database to obtain the identity of the isolate you supplied. Data contained in the MicroSeq™ database has been validated using other microbial identification technologies to ensure the accuracy of identification. NCIMB Ltd is expanding to this database with information generated from its own culture collection of over 13 000 strains. NCIMB Ltd endeavour to obtain a genus or species level match from these databases but should this not be possible publicly available databases such as EMBL and RDP are also searched.

YOUR REPORT

Identification Summary
On the front cover of your report is a summary identification of our analysis of the sequence of your isolate and provides the closest identification we have been able to obtain for your sequence either by MicroSeq™, NCIMB LTD's or the publicly available databases. A percentage match is also provided and our indication of whether this is a genus or species level match.

The data we used to obtain this result is provided in the following pages:

TOP 20
This list highlights the Top 20 hits from the MicroSeq™ Database. The results are shown as % genetic difference in order of closed related to the sequence of your isolate. A match of above 1% is a species level match and between 1 and 3 % is a genus level matches. Matches above 3 % will be searched against other databases.

Phylogenetic Tree
The tree is a pictorial representation of the relationship of your isolates sequence to the sequences in the database. The sum of the horizontal lengths gives the distance between relationships i.e. shorter branch lengths means a closer relationship.

Concise Alignment
This shows the alignment of portions of your sequence with sequences from the database and highlights positions where there are differences. The numbers above the DNA sequence indicate the nucleotide positions and are read vertically top to bottom

EMBL
In the event that your sequence did not produce a genus level match we will have searched the publicly available databases (also you may have asked us to look for a species level match for a genus level match). The results from this search are displayed in an appendix at the back of your report. The format shows the sequence of your isolate aligned with the closest sequence from the EMBL database, nucleotides which are similar are shown with dots between the two sequence, difference are shown by spaces. The percentage similarity is also given.

Please contact us if you have any queries with the interpretation of your report – we are happy to help!

Date Issued: 26/01/2002

PROVIDING THE SOLUTION

NCIMB

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Tel: +44 (0) 1224 273332 Fax: +44 (0) 1224 272461 E-mail enquiries@ncimb.co.uk Website: http://www.ncimb.co.uk

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